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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/685,696 | 10/09/2000 | Tongtong Wang | 210121.455C13 | 3927 |

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Jane E R Potter
Seed Intellectual Property Law Group PLLC
701 Fifth Avenue
Suite 6300
Seattle, WA 98104-7092

| EXAMINER | |
|---|---|
| CHEN, SHIN LIN | |
| ART UNIT | PAPER NUMBER |
| 1632 | |

DATE MAILED: 03/05/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/685,696 | Applicant(s) WANG ET AL. | |
|---|---|---|---|
| | Examiner Shin-Lin Chen | Art Unit 1633 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *14 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-60* is/are pending in the application.

4a) Of the above claim(s) *4-11,16,23-30 and 32-60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,12-15,17 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

1. Applicant's election of group I, claims 1-3, 12-15, 17-22 and 31 and SEQ ID No. 176, in Paper No. 8 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (M.E.P.. § 818.03(a)).

2. Claims 4-11, 16, 23-30 and 32-60 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 8.

Claims 1-60 are pending and claims 1-3, 12-15, 17-22 and 31 are under consideration.

### *Priority*

The priorities of Application Nos. 09/285,479, 09/221,107, 09/123,912, 09/040,802, and PCT US99/05798 are not granted because none of the applications disclose 100% nucleotide sequence of SEQ ID No. 176. Thus, the effective priority date of SEQ ID No. 176 of the present application is the filing date of application No. 09/466,396, i.e. 12-17-99.

### *Claim Rejections - 35 USC § 112*

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1, 2, 12-15, 17-22 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "moderately stringent conditions" in claim 1 is vague and renders the claim indefinite. It is unclear as to the metes and bounds of what would be considered "moderately stringent conditions". The specification fails to specifically define the phrase "moderately stringent conditions". Claims 2, 12-15, 17-22 and 31 depend on claim 1 but fail to clarify the indefiniteness.

***Claim Rejections - 35 USC § 101 & 112***

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 12-15, 17-22 and 31 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

The claimed invention is drawn to an isolated polypeptide comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, comprising amino acid sequence encoded by (a) a polynucleotide sequence of SEQ ID No. 175, (b) a polynucleotide sequence that hybridizes to the sequence of SEQ ID No. 175, or (c) complements of sequences of (a) or (b), or a polypeptide sequence comprising SEQ ID No. 176, a fusion protein comprising the polypeptide sequence set forth above, a pharmaceutical composition comprising said polypeptide or fusion protein, a vaccine comprising said polypeptide or fusion protein, and a method for inhibiting the development of a cancer in a patient by administering to said patient said pharmaceutical composition or said vaccine. The specification states that the amino acid sequence of SEQ ID No. 176 is encoded by the polynucleotide sequence of SEQ ID NO. 175, which is a full-length cDNA sequence of L523S clone.

Although the specification indicates that SEQ ID No. 176 or its variant can be used as an immunogen to produce antibody or immune response, used as a marker for the progression of a cancer, or used for immunotherapy of cancer, such as lung cancer (specification, p. 78, 100, 109), the specification fails to provide a specific and substantial utility for the putative amino acid sequence of SEQ ID No. 176, or its variant, encoded by SEQ ID No. 175 because of the following reasons:

Firstly, no sequence comparison of the amino acid sequence of SEQ ID No. 176 with other polypeptide sequence has been provided. It is unclear what would be the function of the polypeptide of SEQ ID NO. 176. The specification fails to provide any information concerning

the biological function of the polypeptide of SEQ ID No. 176. No polypeptide has been produced from the polynucleotide sequence of SEQ ID No.175, and no function or biological activity of said polypeptide has been provided in the present application.

Secondly, it is unclear whether SEQ ID No. 176 or its variant is differentially expressed in cancer cells, such as lung cancer cells, as compared to normal cells. Although polynucleotide sequence of SEQ ID No. 175 was isolated by subtractive hybridization of a human normal lung cDNA library from a human lung squamous cell carcinoma cDNA library, no evidence has been provided that polypeptide sequence of SEQ ID No. 176 or its variant is expressed at higher level in cancer cells, such as lung cancer cells, as compared to normal cells. It is unclear whether the polypeptide sequence of SEQ ID No. 176 or its variant can be used as a marker for cancer progression, or used to stimulate immune response for immunotherapy of a cancer without knowing the polypeptide sequence of SEQ ID No. 176 or its variant is indeed expressed at higher level in cancer cells, such as lung cancer cells, as compared to normal cells and/or without knowing the biological function of SEQ ID No. 176 or its variant. Using the polypeptide of SEQ ID No. 176 or fragment thereof to produce antibody is not considered a specific and substantial utility because no specific disease or disorder could be associated with the putative polypeptide of SEQ ID No. 176.

In view of the lack of support from the specification on the biological activity for the putative polypeptide of SEQ ID No. 176 and the lack of support for the association of said polypeptide with a particular disease or disorder, such as cancer, it is unclear what kind of

biological activity could be attributed to said polypeptide. Therefore, no specific and substantial utility could be ascribed to the claimed polypeptide in the present application.

7. Claims 1-3, 12-15, 17-22 and 31 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The claimed invention is drawn to an isolated polypeptide comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, comprising amino acid sequence encoded by (a) a polynucleotide sequence of SEQ ID No. 175, (b) a polynucleotide sequence that hybridizes to the sequence of SEQ ID No. 175, or (c) complements of sequences of (a) or (b), or a polypeptide sequence comprising SEQ ID No. 176, a fusion protein comprising the polypeptide sequence set forth above, a pharmaceutical composition comprising said polypeptide or fusion protein, a vaccine comprising said polypeptide or fusion protein, and a method for inhibiting the development of a cancer in a patient by administering to said patient said pharmaceutical composition or said vaccine. The specification states that the amino acid sequence of SEQ ID No. 176 is encoded by the polynucleotide sequence of SEQ ID NO. 175, which is a full-length cDNA sequence of L523S clone.

The claims encompass a genus of various structural variants of polypeptide sequence of SEQ ID No. 176. A polypeptide comprising at least an immunogenic portion of SEQ ID No. 176

or a variant thereof, or a polypeptide comprising at least an immunogenic portion of an amino acid sequence encoded by polynucleotide sequence that hybridizes to SEQ ID No. 175 under moderate stringent conditions would encompass numerous unknown and unidentified polypeptides that differ dramatically from the sequence of SEQ ID No. 176. Especially, the polynucleotide sequence that hybridizes to SEQ ID No. 175 could have a high homologous region but the rest of the polynucleotide sequence could be totally different from SEQ ID No. 175, and thus encodes a very different polypeptide sequence from SEQ ID No. 176.

As per the section 101 rejection above, the specification fails to provide evidence that the putative polypeptide of SEQ ID No. 176 has any biological function. The claimed invention is not enabled in view of the lack of teachings in the specification as filed regarding what amino acid residue(s) could be deleted, substituted, or added to SEQ ID No. 176, such that an asserted utility would be recognized as specific and substantial. It is not apparent that one skilled in the art would know how to use the claimed invention, since as argued previously, no function can be ascribed to the amino acid sequence of SEQ ID No. 176, and since no specific and substantial utility can be ascribed to the claimed polypeptides. In view of the fact that there is no specific guidance or teachings for such in the specification as filed, it would require one skilled in the art at the time of the invention undue experimentation to practice over the full scope of the invention claimed.

Further, the specification also fails to provide adequate guidance for a domain or a region within the putative polypeptide of SEQ ID No. 176 that contributes to any functional

characteristic of said polypeptide. There is no indication of regions or specific amino acids within the polypeptide of SEQ ID No. 176 where mutations or variations would be tolerated without any change of the functional characteristic of said polypeptide and regions where they would not be tolerated. The amino acid sequence of a protein determines its structural and functional properties, and predictability of which amino acids can be removed from a protein's sequence and still result in similar activity is extremely complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's structure from mere sequence data are limited. Rudinger, 1976 (Peptide Hormones, Edited by Parsons, University Park Press, Baltimore, p. 1-7), points out that "The significance of particular amino acids and sequences for different aspects of biological activity cannot be predicted *a priori* but must be determined from case to case by painstaking experimental study" (e.g. p. 6). Kaye et al., 1990 (Proc. Natl. Acad. Sci. USA, Vol. 87, pp. 6922-6926) teaches that "A single amino acid substitution results in a retinoblastoma protein defective in phosphorylation and oncoprotein binding" (e.g. Title). Skolnick et al., 2000 (Trends in Biotech, Vol. 18, p. 34-39) states "Sequence-based methods for function prediction are inadequate because of the multifunctional nature of proteins. However, just knowing the structure of the protein is also insufficient for prediction of multiple functional sites. Structural descriptors for protein functional sites are crucial for unlocking the secrets in both the sequence and structural-genomics projects" (e.g. abstract). Skolnick further states that "Knowing a protein's structure does not necessarily tell you its function" and "Because proteins can have similar folds but different functions,

determining the structure of a protein may or may not tell you something about its function" (e.g. p. 36, box 2). In view of the lack of detailed information regarding the structural and functional requirements of the polypeptide of SEQ ID No. 176 and its variants, and the unpredictability of polypeptide function from mere amino acid sequence, it would be unpredictable what would be the biological function of SEQ ID No. 176 from mere amino acid sequence and whether the polypeptide variants of SEQ ID No. 176 would have same functional characteristics, if any, as the polypeptide of SEQ ID No. 176 disclosed in the present application.

In addition, the complement of polynucleotide sequence of SEQ ID No. 175 or the complements of polynucleotide sequences that hybridize to SEQ ID No. 175 under moderate stringent conditions have totally different polynucleotide sequences as compared to SEQ ID No. 175 or sequences that hybridize to SEQ ID No. 175 and those complements do not necessarily encode a polypeptide. Even those complements encode polypeptide sequences, said polypeptide sequences could vary dramatically different from SEQ ID No. 176. The specification fails to provide an enabling disclosure that complements of polynucleotide sequence of SEQ ID No. 175 or the complements of polynucleotide sequences that hybridize to SEQ ID No. 175 under moderate stringent conditions do encode polypeptides and said polypeptides have biological functions. One skilled in the art at the time of the invention would not know how to use the polypeptides, if any, encoded by the complements set forth above.

Therefore, it is concluded that based upon the nature of the claimed invention, the state of the art, the unpredictability found in the art, the teaching and working examples provided, and

the breadth of the claims that it would require one skilled in the art at the time of the invention undue experimentation to practice over the full scope of the invention claimed.

***Claim Rejections - 35 USC § 112***

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-3, 12-15, 17-22 and 31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed invention is drawn to an isolated polypeptide comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, comprising amino acid sequence encoded by (a) a polynucleotide sequence of SEQ ID No. 175, (b) a polynucleotide sequence that hybridizes to the sequence of SEQ ID No. 175, or (c) complements of sequences of (a) or (b), or a polypeptide sequence comprising SEQ ID No. 176, a fusion protein comprising the polypeptide sequence set forth above, a pharmaceutical composition comprising said polypeptide or fusion protein, a vaccine comprising said polypeptide or fusion protein, and a method for inhibiting the development of a cancer in a patient by administering to said patient said pharmaceutical composition or said vaccine. The specification states that the amino acid

sequence of SEQ ID No. 176 is encoded by the polynucleotide sequence of SEQ ID NO. 175, which is a full-length cDNA sequence of L523S clone.

The claims encompass a genus of various structural variants of polypeptide sequence of SEQ ID No. 176. A polypeptide comprising at least an immunogenic portion of SEQ ID No. 176 or a variant thereof, or a polypeptide comprising at least an immunogenic portion of an amino acid sequence encoded by polynucleotide sequence that hybridizes to SEQ ID No. 175 under moderate stringent conditions would encompass numerous unknown and unidentified polypeptides that differ dramatically from the sequence of SEQ ID No. 176.

The scope of the claim includes a genus of numerous structural variants of SEQ ID No. 176, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Therefore, structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of SEQ ID No. 176 is insufficient to describe the genus.

This limited information is not sufficient to reasonably convey to one skilled in the art that applicants were in possession of numerous variants of SEQ ID No. 176 as claimed in the

present invention. Thus it is concluded that the written description requirement is not satisfied for the genus.

***Claim Rejections - 35 USC § 102***

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Mueller-Pillasch et al., 1997 (SPTREMBL Accession No. O00425).

Claim 1-3 are directed to an isolated polypeptide comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, comprising amino acid sequence encoded by (a) a polynucleotide sequence of SEQ ID No. 175, (b) a polynucleotide sequence that hybridizes to the sequence of SEQ ID No. 175, or (c) complements of sequences of (a) or (b), or a polypeptide sequence comprising SEQ ID No. 176.

Mueller-Pillasch teaches a human putative RNA binding protein KOC polypeptide sequence, SPTREMBL Accession No. O00425, which is 100% identical to SEQ ID No. 176. The polynucleotide sequence (Mueller-Pillasch, GenEmbl Accession No. U97188) encoding the polypeptide sequence of SPTREMBL Accession No. O00425 is 100% identical to SEQ ID No. 175. Thus, claims 1-3 are clearly anticipated by Mueller-Pillasch.

***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. The examiner can normally be reached on Monday to Friday from 9 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Scott Priebe can be reached on (703) 308-7310. The fax phone number for this group is (703) 308-4242.

Questions of formal matters can be directed to the patent analyst, Patsy Zimmerman, whose telephone number is (703) 305-2758.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Shin-Lin Chen, Ph.D.